REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

The claims have been amended to more particularly point out and distinctly claim the subject matter of this invention. Claims 35, 37, 38, 39, 41, 43, 45, 47, and 50-54 have been canceled. New claims 57-60 are added. Claims 34, 36, 40, 42, 44, 46, 48-49, and 55-60 are pending after the foregoing amendments.

The specification has been amended to reference the SEQ ID NOS of the Sequence Listing submitted on March 9, 1998. Since the Examiner has indicated that the CFR is suitable, an identical paper copy of the Sequence Listing filed on March 9, 1998 is submitted herewith, in order to avoid unnecessary expense to this small entity applicant. The nucleic acids pointed out by the Examiner on pages 18 and 19 are set forth in the Sequence Listing as SEQ ID NOS: 37-39.

The invention relates to the identification of a W chromosome-linked gene in birds. The gene is termed "CHD-W" because of its sequence similarity to the known CHD-1 gene from mouse. An autosomal (i.e. non-sex-linked) form of the gene in birds is also identified ("CHD-1A"). The inventors have (i) identified a bird CHD gene, not previously known to exist, and (ii) enabled methods for determining the sex of birds based on testing for the presence or absence of CHD-W gene sequences in a DNA sample.

Claims 34-39 are rejected under 35 USC 112, first paragraph, on the basis that the claims do not satisfy the written description requirement. This ground of rejection is respectfully traversed as applied to the claims after the foregoing amendments.

This ground of rejection is deemed to be overcome by amendment of claim 34 replacing the term "comprising" with "consisting of", corresponding to allowed claim 55.

Claims 35, 37, 39, 41, 43, 45, and 47-49 are rejected under 35 USC 112, first paragraph, as lacking enablement. This ground of rejection is respectfully traversed as applied to the claims after the foregoing amendments.

The Examiner alleges that the specification is only enabling for methods of determining the sex of a bird comprising hybridising the disclosed polynucleotides to DNA of a bird which has been

digested with a restriction enzyme. In response, claims 35, 37, 39, 41, 43, 45, and 47 are cancelled, and claims 36, 44, 48 and 49 have been amended to recite said feature.

On page 8 of the Office Action the Examiner appears to object to claims 48 and 49 as reciting the use of the method on DNA or RNA of a bird when there is no teaching in the specification as to how to distinguish between RNAs transcribed from CHD-1A and CHD-W genes.

If such position is being asserted by the Examiner, such position is respectfully traversed. A person of ordinary skill in the art can easily apply the teaching of the application to both DNA and RNA by routine methods and without exercising any inventive effort or undue experimentation. To restrict the claims to DNA alone would be to unduly limit the protection which should be afforded to the Applicant.

Claims 34-49 are rejected under 35 USC 112, second paragraph, on the basis that the polynucleotide claims presently on file are directed to bird CHID gene sequences and, therefore, do not encompass the mouse CHD-1 sequence.

SEQ ID No. 2 has accordingly been deleted from the claims. Thus this ground of rejection is deemed to be overcome.

Claims 36, 37 and 40-47 are rejected under 35 USC 102 as being anticipated by Delmas et al. for the reasons set forth.

This ground of rejection is deemed to be overcome by incorporation of the subject matter of non-rejected claim 38 into claim 36.

In addition, claim 42 has been amended to require that the isolated polynucleotide hybridises under high stringency conditions to the polynucleotide according to claim 34.

Delmas does not disclose an isolated polynucleotide which hybridises under high stringency conditions with the polynucleotides of claim 34 (i.e. having about 90% homology to a polynucleotide of claim 34).

Lastly, claims 36, 37 and 40-47 are rejected under 35 USC 103 as being unpatentable over Delmas et al. in view of Dresser for the reasons set forth. This ground of rejection is respectfully traversed.

The cited references fail to suggest the invention of the amended and new claims.

Accordingly, favorable reconsideration and allowance is solicited.

A marked-up version of the amendments to the specification and claims is attached.

Respectfully submitted,

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SPECIFICATION AMENDMENTS

Page 4, paragraph on lines 2-8:

It is believed that all birds such as chickens and other species of commercial significance, will have two or more genes of the CHD type which will have a nucleotide sequence similar to the nucleotide sequences shown in Fig. 5 (SEQ ID NO: 10), Fig. 7 (SEQ ID NOS: 11-14) and Fig. 8 (SEQ ID NO: 15) and that the gene products will be proteins which are crucial to the determination of the sex of the organism. One of these genes will be located on the W chromosome and the other on an autosome or Z chromosome.

Page 8, paragraph on lines 24-28:

The invention particularly provides an oligonucleotide, polypeptide, nucleic acid or protein comprising the entire sequence of the CHD-gene of a bird and more preferably comprising the entire amino acid or nucleotide sequence of the chicken as set out in any one of Fig. 1 (SEQ ID NO: 1), Fig. 3 (SEQ ID NOS: 2-9), Fig. 5 (SEQ ID NO: 10), Fig. 7 (SEQ ID NOS: 11-14), Fig. 8 (SEQ ID NO: 15), Fig. 9 (SEQ ID NOS: 16-19), Fig. 10 (SEQ ID NOS: 20-21), and Fig. 11 (SEQ ID NOS: 22-30).

Page 14, paragraph on lines 17-21:

In addition, the nucleotide sequence of the CHD-genes are sufficiently conserved so that CHD primers can be designed that will allow PCR in a range of bird species. The primers P1 (SEQ ID NO: 37), P2 (SEQ ID NO: 39) and P3 (SEQ ID NO: 38) shown in Figure 14 will allow CHD-W and CHD-1A amplification in a range of birds that allows sex to be identified.

Page 27, paragraph on lines 2-14:

The procedure was published in Griffiths & Tiwari (1995) which covers the extraction of the DNA. The second test was to provide DNA from a Hyacinth Macaw which would yield data to allow construction of primers. A IFIX II library was provided by Stratagene and this was probed with the insert of the *CHD-1A* clone Z6 (-227-5302 Fig. 6) at moderate stringency. This provided 7 positive clones (A1, A2, A7, A8, A13, 1.2 and 5C). The inserts were extracted cut with *Mbol* and subcloned into the *Baml* cut pUC18. This sublibrary was probed again with the Z6 insert but this time at high stringency. The A12.3 subclone hybridized. This was sequenced (SEQ ID NO: 36) and contained 111bp which is aligned to the chicken and mouse CHD genes (SEQ ID NOS: 31, 32 and 34) in Fig.

14. The similarity of this fragment to the chicken *CHD-W* suggested this was the Hyacinth Macaw homologue of the W chromosome located gene.

Page 27, paragraph on lines 15-29:

The data from A12.3 supplied information for the design of the primers required. It also provided evidence that the CHD sequences were sufficiently conserved in this region that a single set of primers could be designed to amplify both genes. Three primers, P1, P2 and P3 were designed to allow seminested PCR (Fig. 14). This technique allowed amplification of a 104 bp region of both *CHD-W* (SEQ ID NO: 35) and *CHD-1A* (SEQ ID NO: 33) from DNA that was available from two captive Spix's Macaws of known sex. In each sex the PCR products were of the same size but sequence determination revealed that the *CHD-W* derived PCR product possessed a *DdeI* restriction enzyme site which was lacking in the *CHD-1A* product. Thus PCR amplification and *DdeI* cleavage of male Spix's Macaw DNA yields a only single product of 104 base pairs (bp), whilst from female DNA two products are apparent, one of 104 bp and one of 73 bp. The presence of the *CHD-1A* product in both sexes acts as a control to ensure the PCR amplification has been successful (Fig 15 & 16).

Twice

36. (Amended) A fragment of the polynucleotide according to claim 34, which gives a specific signal only on the W chromosome upon hybridisation to the genomic DNA of a non-ratite bird, wherein said genomic DNA has been digested with a restriction endonuclease.

Twice

42. (Amended) An isolated polynucleotide which hybridises under ~~moderate to~~ high stringency conditions to the polynucleotide according to claim 34.

~~43. (Amended) An isolated polynucleotide which hybridises under moderate to high stringency conditions to the polynucleotide according to claim 35.~~

Twice

44. (Amended) The polynucleotide according to claim 42, which gives a specific signal only on the W chromosome upon hybridisation to the genomic DNA of a non-ratite bird, wherein said genomic DNA has been digested with a restriction endonuclease.

~~45. (Amended) The polynucleotide according to claim 43, which gives a specific signal only on the W chromosome upon hybridisation to the genomic DNA of a non-ratite bird.~~

46. (Amended) The polynucleotide according to claim 44, wherein the non-ratite bird is selected from the group consisting of chicken, turkey, duck and parrot.

~~47. (Amended) The polynucleotide according to claim 45, wherein the non-ratite bird is selected from the group consisting of chicken, turkey, duck and parrot.~~

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(ii) subjecting (a), (b) or (c) to restriction endonuclease digestion wherein the restriction endonuclease digestion yields hybridisable fragments of CHD-W which are of a different size to those of CHD1-A,

(iii) hybridising the polynucleotide according to claim 34 or a fragment thereof with the product of step (ii) under moderate to high stringency conditions, and

Twice

48. (Amended) A method for determining the sex of a non-ratite bird or of an embryo, fetus, cell or tissue of a non-ratite bird, which comprises:

(i) obtaining

~~hybridising under moderate to high stringency conditions the polynucleotide according to claim 34 or 35 with~~ either

(a) a DNA or RNA of the non-ratite bird, embryo, fetus, cell or tissue thereof or,

(b) a cDNA reverse transcribed from RNA of the non-ratite bird, embryo, fetus, cell or tissue thereof, or

(c) a cDNA or DNA amplified by cloning or polymerase chain reaction from DNA or RNA of the non-ratite bird, embryo, fetus, cell of tissue thereof, ~~and~~

(iv) detecting the size of restriction fragments to which the polynucleotide hybridises ~~presence or absence of hybridisation of the polynucleotide to (a), (b) or (c),~~ which result is indicative of the sex of the non-ratite bird, embryo, fetus, cell or tissue thereof.

Twice

49. (Amended) A method for determining the sex of a non-ratite bird or of an embryo, fetus, cell or tissue of a non-ratite bird, which comprises:

(i) hybridising

~~hybridising under moderate to high stringency conditions the polynucleotide according to claim 42 or 43 with~~ either

(a) a DNA or RNA of the non-ratite bird, embryo, fetus, cell or tissue thereof or,

(b) a cDNA reverse transcribed from RNA of the non-ratite bird, embryo, fetus, cell or tissue thereof, or

(c) a cDNA or DNA amplified by cloning or polymerase chain reaction from DNA or RNA of the non-ratite bird, embryo, fetus, cell or tissue thereof, ~~and~~

(ii) subjecting (a), (b) or (c) to restriction endonuclease digestion wherein the restriction endonuclease digestion yields hybridisable fragments of CHD-W which are of a different size to those of CHD1-A,

(iii) hybridising the polynucleotide according to claim 42 or a fragment thereof with the product of step (ii) under moderate to high stringency conditions, and

size of restriction fragments to which the polynucleotide hybridises

detecting the ~~presence or absence of hybridisation of the polynucleotide to (a), (b) or (c)~~

which result is indicative of the sex of the non-ratite bird, embryo, fetus, cell or tissue thereof.

(Amended)

55. An isolated polynucleotide consisting of the nucleotide sequence set forth in SEQ ID No. 1, ~~2~~, 3, 4, 5, 10, 12, 13, or 15.